

### **REMARKS**

Claims 1-23 are pending. By virtue of this response, claim 1 is amended. Claims 17-23 are withdrawn. Therefore, claims 1-16 are presently under examination. Amendment and cancellation of certain claims is not to be construed as a dedication to the public of any of the subject matter of the claims as previously presented. No new matter is added.

#### **I. Claim Objections**

Claim 1 is objected to because of the following informalities: on first sight the acronym “OMV” should be followed by “Outer Membrane Vesicle”. Applicants have amended claim 1 to recite “outer membrane vesicles (OMVs)”. Applicants therefore respectfully request the withdrawal of the objection to claim 1.

#### **II. Claim Rejections Under 35 USC §102**

Claims 1-4 and 10-13 are rejected under 35 U.S.C. 102(b) as allegedly being anticipated by Fukasawa *et al.* (Vaccine, 1999; 17: 2951-2958).

Applicant respectfully traverses the rejection and its supporting remarks. Fukasawa *et al.* fail to teach “a step of ultrafiltration of ***a crude OMV preparation*** containing bacterial DNA ***prior to*** any ultracentrifugation or ***sterilisation steps***.” Fukasawa *et al.* fails to teach this limitation for two reasons. First, the cells were heated to 54 °C to “inactivate” them. Thus, the cells were subject to a sterilization step prior to the diafiltration. Second, the diafiltration step after heating to 54 °C was not with “a crude OMV preparation”. The diafiltration step was performed on the heat killed whole *Neisseria* cells. The cells were not disrupted to create a crude OMV preparation until addition of deoxycholate, which is the detergent typically used to disrupt the *Neisseria* outer membrane to form OMVs. Fukasawa *et al.* only added deoxycholate to create a crude OMV preparation as part of the ultracentrifugation step. Thus, Fukasawa *et al.* fail to anticipate the pending claims.

Applicant therefore respectfully requests the withdrawal of the rejection of claims 1-4 and 10-13.

**III. Claim Rejections Under 35 USC §103 – Fukasawa and Berthet**

Claims 1-7 and 10-15 are rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Fukasawa et al. (Vaccine, 1999; 17: 2951-2958), and further in view of Berthet et al. (U.S. Publication 2006/0204520 A1; Filed: 2/8/02).

Applicants respectfully traverse the rejection and its supporting remarks. As discussed above, for at least two reasons, Fukasawa *et al.* fail to teach “a step of ultrafiltration of ***a crude OMV preparation*** containing bacterial DNA ***prior to*** any ultracentrifugation or ***sterilisation steps.***” The Examiner has not established that Berthet *et al.* remedy this deficiency. Therefore the pending claims are not obvious.

Applicant therefore respectfully requests the withdrawal of the rejection of claims 1-7 and 10-15.

**IV. Claim Rejections Under 35 USC §103 – Granoff and van Reis**

Claims 1, 2, 4, 5, 8-13 and 16 are rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Granoff et al. (U.S. Patent 6,936,261 B2; Filed 7/27/01) and further in view of van Reis et al. (Current Opinion in Biotechnology, 2001; 12: 208-211).

Applicants respectfully traverse the rejection and its supporting remarks. The Examiner appears to be re-raising essentially the same art (Granoff *et al.* US2006/002921) that the Examiner had previously rejected the pending claims as allegedly being anticipated by in this obviousness rejection. According to PublicPAIR, US2006/002921 is a continuation of U.S. Patent 6,936,261, so the specifications should have the same disclosure. In fact the Examiner has cited to the same text for this obviousness rejection. As will be explained below, van Reis *et al.* do not remedy any of the deficiencies noted in the Applicants arguments in the Pre-Appeal Brief Arguments, which lead to the Examiner’s withdrawal of the anticipation rejection.

A *prima facie* case of obviousness must expressly or inherently teach or suggest all of the claimed elements.

A. *Granoff et al. and van Reis et al. do not Expressly Teach Ultrafiltration of a Crude OMV Preparation Containing Bacterial DNA*

Granoff *et al.* do not expressly teach the claimed “step of ultrafiltration of a crude OMV preparation *containing bacterial DNA*”. Similarly, van Reis *et al.* do not expressly teach that ultrafiltration may be performed in the presence of contaminating “*bacterial DNA*”. The Examiner has asserted that the single sentence in Col. 14, lines 19-35, renders the claimed invention obvious when combined with van Reis *et al.* However, nowhere in the single sentence pointed to by the Examiner do Granoff *et al.* teach that a crude OMV preparation *containing bacterial DNA* is subject to ultrafiltration. The sentence does not mention how to deal with bacterial DNA at all and only references filtration (not ultrafiltration specifically) among a number of techniques that may generally be used, which is a broad category of techniques only one of which is filtration. Filtration includes sterile filtration with 0.22  $\mu\text{m}$  filters, which is clearly not ultrafiltration. There is no detail about how to actually implement any of these broad categories of techniques such as whether preliminary processing would be required before use of the technique (*e.g.*, removal of bacterial DNA and other cellular debris). Thus, Granoff *et al.* does not *expressly* teach this element of the pending claims the pending claims.

van Reis *et al.* fail to remedy the above deficiencies as van Reis *et al.* do not teach that HPTFF can be performed on crude OMV preparations without first removing the bacterial DNA. In fact, van Reis *et al.* teach that “[a] limitation of the technology [HPTFF] is the susceptibility to fouling by feed streams containing precipitates.” Thus, one of skill in the art reading van Reis *et al.* would most likely perform an initial step to remove bacterial DNA to prevent the viscous DNA from fouling the filter. Thus, the combination of Granoff *et al.* and van Reis *et al.* do not expressly teach ultrafiltration of a crude OMV preparation *containing bacterial DNA* and van Reis *et al.* actually teaches away from the claimed method by teaching that HPTFF are susceptible to fouling.

Moreover, the advantages cited by the Examiner asserting that one of skill in the art would use HPTFF as taught by van Reis *et al.* are all directed to the utility of HPTFF in purifying proteins. OMVs are not proteins. OMVs are much, much larger lipid vesicles that include membrane proteins in the lipid membrane of the vesicles.

B. *Granoff et al. and van Reis et al. do not Inherently Teach Ultrafiltration of a Crude OMV Preparation Containing Bacterial DNA*

Since Granoff *et al.* and van Reis *et al.* together do not expressly teach the above elements, the only way Col. 14, lines 19-35 of Granoff *et al.* could render the pending claims obvious is if this single sentence together with van Reis *inherently* teaches ultrafiltration of a crude OMV preparation **containing bacterial DNA**. MPEP 2112(IV) sets out the requirements for inherent anticipation as:

The fact that a certain result or characteristic *may* occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *In re Rijckaert*, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993) (reversed rejection because inherency was based on what would result due to optimization of conditions, not what was necessarily present in the prior art); *In re Oelrich*, 666 F.2d 578, 581-82, 212 USPQ 323, 326 (CCPA 1981). “To establish inherency, the extrinsic evidence ‘must make clear that the missing descriptive matter is **necessarily present** in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, **may not be established by probabilities or possibilities**. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.’” *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999) (citations omitted) ...

Thus, even if one of skill in the art were so bold as to attempt to purify OMVs based solely upon the single sentence of Granoff *et al.*, it is not enough that it *may* lead to ultrafiltration of a crude OMV preparation **containing bacterial DNA**. One of skill in the art practicing this single sentence even if using HTPFF taught by van Reis must **necessarily** perform “a step of ultrafiltration of a crude OMV preparation containing bacterial DNA prior to any ultracentrifugation or sterilisation steps.” The burden to establish inherency is clearly on the Examiner. Thus, unless the Examiner can provide evidence or sound reasoning that one of skill in the art would follow this single sentence of Granoff *et al.* and necessarily perform HTPFF of a crude OMV preparation **containing bacterial DNA**, the Examiner has not established that Granoff *et al.* when combined with van Reis *et al.* inherently renders the claimed invention obvious.

Granoff *et al.* when combined with van Reis *et al.* do not expressly teach or suggest all of the claimed elements and do not inherently teach or suggest all of the claimed elements. Therefore Granoff *et al.* when combined with van Reis *et al.* do not render the present claims obvious.

Applicant therefore respectfully requests the withdrawal of the rejection of claims 1, 2, 4, 5, 8-13 and 16.

**V. Claim Rejections Under 35 USC §103 – Granoff, van Reis and Berthet**

Claims 6, 7, 14 and 15 are rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Granoff *et al.* (U.S. Patent 6,936,261 B2; Filed 7/27/01) and further in view of van Reis *et al.* (Current Opinion in Biotechnology, 2001; 12: 208-211) as applied to claims 1, 2, 4, 5, 8-13 and 16 above, and further in view of Berthet *et al.* (U.S. Publication 2006/0204520 A1; Filed: 2/8/02).

Applicants respectfully traverse the rejection and its supporting remarks. As discussed above, Granoff *et al.* when combined with van Reis *et al.* do not expressly teach or suggest all of the claimed elements and do not inherently teach or suggest all of the claimed elements. Therefore Granoff *et al.* when combined with van Reis *et al.* do not render the present claims obvious. The Examiner has not established that Berthet *et al.* remedy this deficiency.

Applicant therefore respectfully requests the withdrawal of the rejection of claims 6, 7, 14 and 15.

**CONCLUSION**

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark Office determines that an extension and/or other relief is required, Applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing **Docket No. 223002110300**. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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